

Frequently Asked Questions – Recombinant DNA Research

1. What is the role of the Institutional Biosafety Committee (IBC)?

The IBC is responsible for monitoring and ensuring compliance as well as review and approval of all research projects that involve recombinant DNA materials, including human gene therapy/gene transfer protocols. IBC's were established under the [NIH Guidelines for Research Involving Recombinant DNA Molecules](#) to provide local review and oversight of nearly all forms of research utilizing recombinant DNA. Over time, many institutions have chosen to assign their IBCs the responsibility of reviewing a variety of experimentation that involves biological materials (e.g., infectious agents) and other potentially hazardous agents (e.g., carcinogens). This additional responsibility is assigned entirely at the discretion of the institution. The University of South Alabama's biosafety policy mandates review of all potential biohazardous agents and recombinant DNA research.

USA's IBC is charged with the following responsibilities:

1. Review and approval of ALL research proposals to include all potential biological agents and recombinant DNA.
2. Approval of safety practices
3. Setting biosafety containment levels (Section III-D-2-b, III-D-5; NIH guidelines)
4. Conducting periodic review to ensure compliance – lab inspections are conducted on an annual basis
5. Oversee biosafety training practices
6. Reporting significant problems or violations of the NIH Guidelines
7. Performance of such other functions as deemed necessary by the institution (Section IV-B-2; NIH Guidelines)

2. How often does the IBC meet?

The frequency of IBC meetings is commensurate with the volume of protocols needing review, the nature and risks of the research, and the need for continuing oversight. The committee meets as needed (typically every quarter) and follows the guidelines provided by the NIH Office of Biotechnology Activities (OBA) involving research with recombinant DNA.

3. What research must be registered with the IBC?

The University of South Alabama's policy regarding recombinant DNA activities requires that all Recombinant DNA work conducted must be registered with the Institutional Biosafety Committee.

- All teaching and research protocols using molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell or molecules that result from the replication from those molecules must be registered and reviewed by the IBC.
- Protocols that (a) involve the cloning of toxin molecules (LD50<100 ng/Kg body weight) or (b) transfer of a drug resistant trait to microorganisms that are not known to acquire the resistance naturally will require the triplicate approvals of: NIH (OBA), the Environmental Health and Safety (EHS) Office, and the IBC. NIH/OBA: <http://www4.od.nih.gov/oba/rac/aboutrdagt.htm> and EHS: <http://www.ehs.pitt.edu/> NIH Guidelines: <http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>
- Work involving animals must also be reviewed and approved by the Institutional Animal Care and Use Committee, see: <http://www.southalabama.edu/com/research/animalcare/index.shtml> or call 460-6308.
- Any modification to a currently approved rDNA research project must be approved through the IBC.

4. How does the IBC review protocols?

The IBC review process:

1. All protocols are received through the Office of Research Compliance and Assurance where they are initially screened to ensure that applications are complete.
2. Complete protocols are entered into the biosafety database and issued a protocol number.
3. Exempt category registrations are administratively reviewed and approved by the IBC chair and reported at the next convened IBC meeting.
4. All biohazardous agents and rDNA registrations are reviewed by the IBC. The IBC typically meets on a quarterly or as-needed basis. In the event a new registration is submitted for review shortly after a convened meeting, the application may be distributed to all committee members for review and vote by mail. The committee will take one of the following possible actions: a) approved, b) approved provided that recommendations are satisfied, c) deferred - pending additional review by reviewer, d) abstain or e) disapprove. In order for a vote by mail to be valid, all members must agree that a convened committee discussion is not needed for review of the registration.
5. Recommendations and/or concerns from the committee are relayed to the investigator through the Office of Research Compliance and Assurance
6. The IBC will review registrations at convened meetings with a quorum present (>50% member attendance)
7. The investigator is notified by the Office of Research Compliance and Assurance of the outcome of the committee's review.

5. What is reviewed by the committee?

The IBC review process considers the following points:

- [Independent determination of BSL appropriate to research proposal
 1. vectors and host systems used in the proposal
 2. safety
 3. environmental considerations
- [Evaluation of facilities, procedures, practices, training of personnel
- [Ensuring compliance with Appendix M of the NIH guidelines (if applicable to the proposal)
- [Assurance that no clinical trial participants are enrolled until RAC (Recombinant Activities Committee, through OBA) review process is complete (when applicable).
- [Consideration of issues and recommendations made by RAC for clinical trial proposals and the Investigator's response to RAC's recommendations (when applicable).
- [Withholding institutional approval of the proposal until after RAC review process has been completed, and the appropriate documentation has been received by both the Investigator and the IBC-rDNA (when applicable).
- [Ensuring compliance with data reporting, adverse event reporting, and surveillance.

6. How to Determine Risk Group and Biosafety Level Containment?

Risk Group (NIH Guidelines)	Containment Level	Examples
RG1: Agents are NOT associated with disease in healthy adult humans	<u>BSL1:</u> <ul style="list-style-type: none"> - Work is done on open bench - top/special containment is not required - Standard microbiological practices - Biohazard signs to be posted 	Escherichia coli K12 and it's derivatives (DH5a, JM109), pBluescript, PYAC4, lambda GT-11 vector

RG2: Agents are associated with human disease which is rarely serious. (moderate risk)	<u>BSL2:</u> <ul style="list-style-type: none"> - All BSL-1 containment and practices PLUS: - Lab access is restricted when work is in progress - Personnel have specific training in handling of agents - Biological safety cabinets or other containment devices are used for potential aerosol generation procedures - Biohazard signs must be posted to include agent/contact information - Specific PPE requirements 	Adenovirus all types All human blood Human cell lines (ie, HEK 293) Herpes simplex virus Herpes virus saimiri Murine retrovirus-based vectors Retroviral packaging cell lines
RG3: Agents are associated with serious or lethal human disease for which preventive or therapeutic interventions MAY be available (high risk)	<u>BSL3:</u> <ul style="list-style-type: none"> - All BSL-2 containment and practices plus the following: - Specific facility design parameters must be followed, including requirements for location, ventilation, room integrity and security 	Industrial scale volumes of Lenti viruses or Lentiviral vectors Rickettsia prowazekii
RG4: Agents are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available.	The university currently does not approve any work at BSL-4 level.	NONE – no current usage of this risk group classification at USA

Viral Vectors	Risk Group/Biosafety Level
Adenovirus	Risk Group 2: BL2
Murine Retrovirus-Ecotropic/Amphotropic or VSV-G pseudotyped	Risk Group 2: BL2
Lentivirus (3 rd generation)**	Risk Group 3: BL2
AAV (w/adenovirus helper)	Risk Group 2: BL2
AAV (helper free)	Risk Group 1: BL2
Herpes virus	Risk Group 2: BL2

** Special requirements – needle protective devices should be used for injection procedures when possible, sealed rotor heads and/or canisters should be used for centrifugation and opened only in a biosafety cabinet, use only ultracentrifuges fitted with HEPA filters.

Screening for Replication Competent Virus- Recombination events or contamination from wildtype virus can result in the presence of replication competent virus (RCV) in a population of replication deficient viral vectors. The IBC recommends testing for the presence of RCV in viral stocks to be used for *in vivo* experiments.

Acknowledgement: Source of information derived from the University of Pittsburg, Recombinant DNA office.